

Endometrial hyperplasia, Uterine carcinoma & Fibroids

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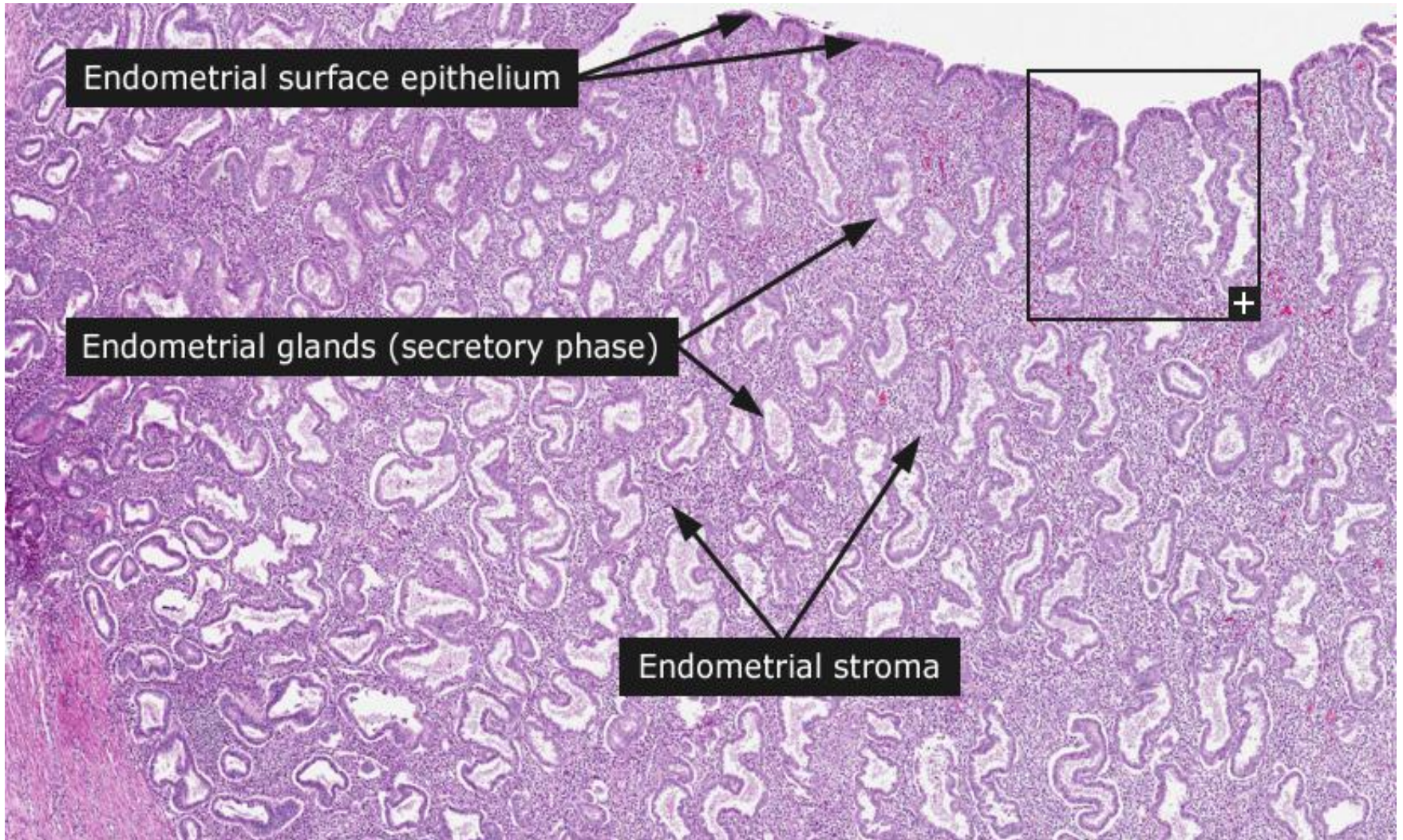
2013-2014

Objective

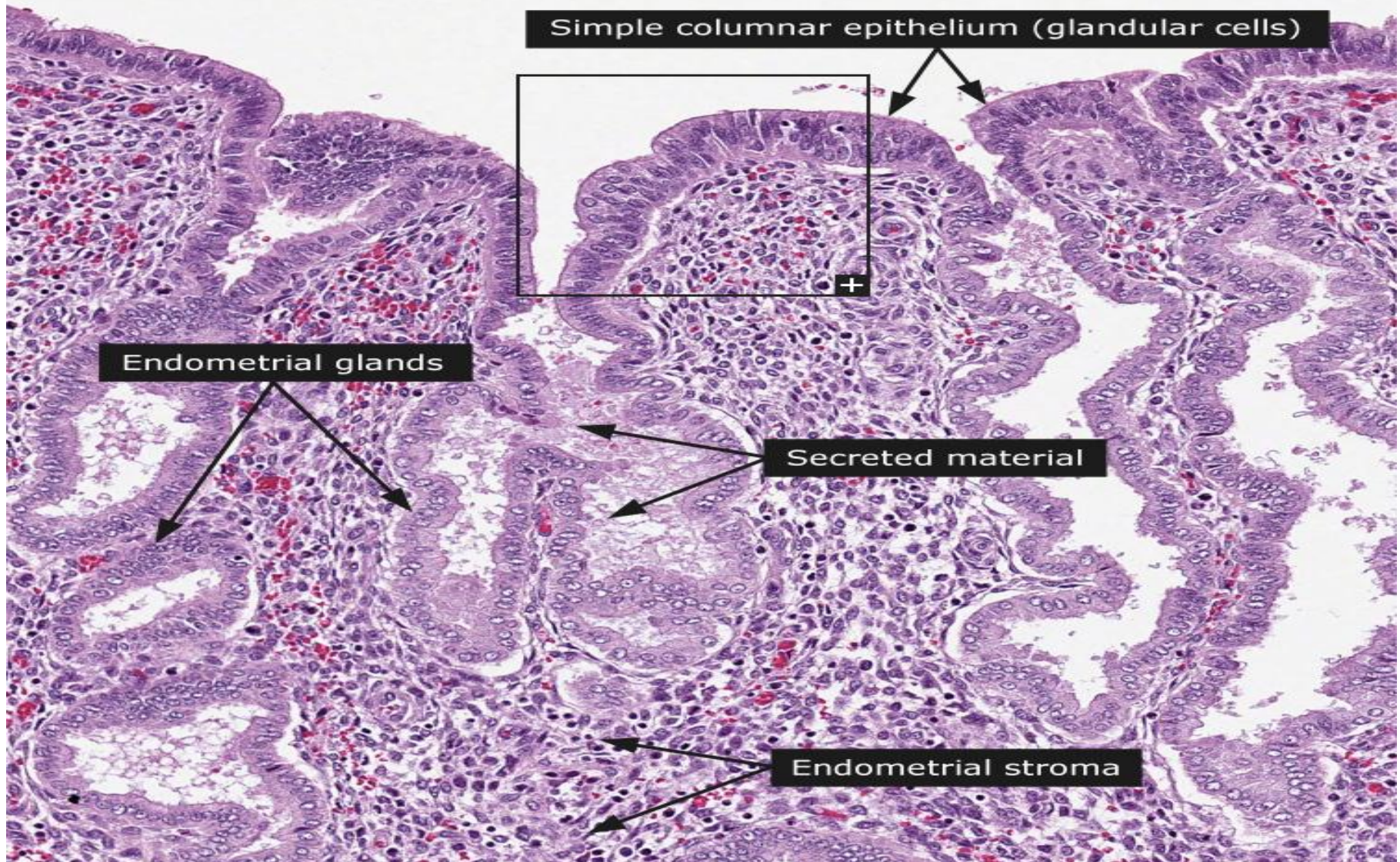
By the end of this lecture the students must be able to :

- Identify the risk factor, types, clinical picture and pathology of Endometrial hyperplasia
- Identify the risk factor, types, clinical picture and pathology of Endometrial carcinoma
- Identify pathology of Endometrial polyps , Leiomyoma & leiomyosarcoma.

NORMAL HISTOLOGY



NORMAL HISTOLOGY



Proliferative Lesions Of The Endometrium & Myometrium

- The most common proliferative lesions of the uterine corpus are endometrial hyperplasia, endometrial carcinomas, endometrial polyps, and smooth muscle tumors.
- All tend to produce abnormal uterine bleeding as their earliest manifestation.

Endometrial hyperplasia

- Exaggerated endometrial proliferation due to **excess of estrogen** .
- The severity of hyperplastic changes is correlated with the level and duration of estrogen excess (exogenous /endogenous).
- Can be pre-neoplastic (**precursor of endometrial carcinoma**)
- It is classified based on architectural crowding (**simple versus complex**) and the presence or absence of **cytologic atypia** into:
 - 1- Simple hyperplasia
 - 2- Complex hyperplasia
 - 3- Atypical hyperplasia
- The risk of developing carcinoma is related to the presence of cellular atypia.
- Also acquisition of **PTEN tumor suppressor gene mutations** is one of key steps in the transformation of hyperplasias to endometrial carcinomas

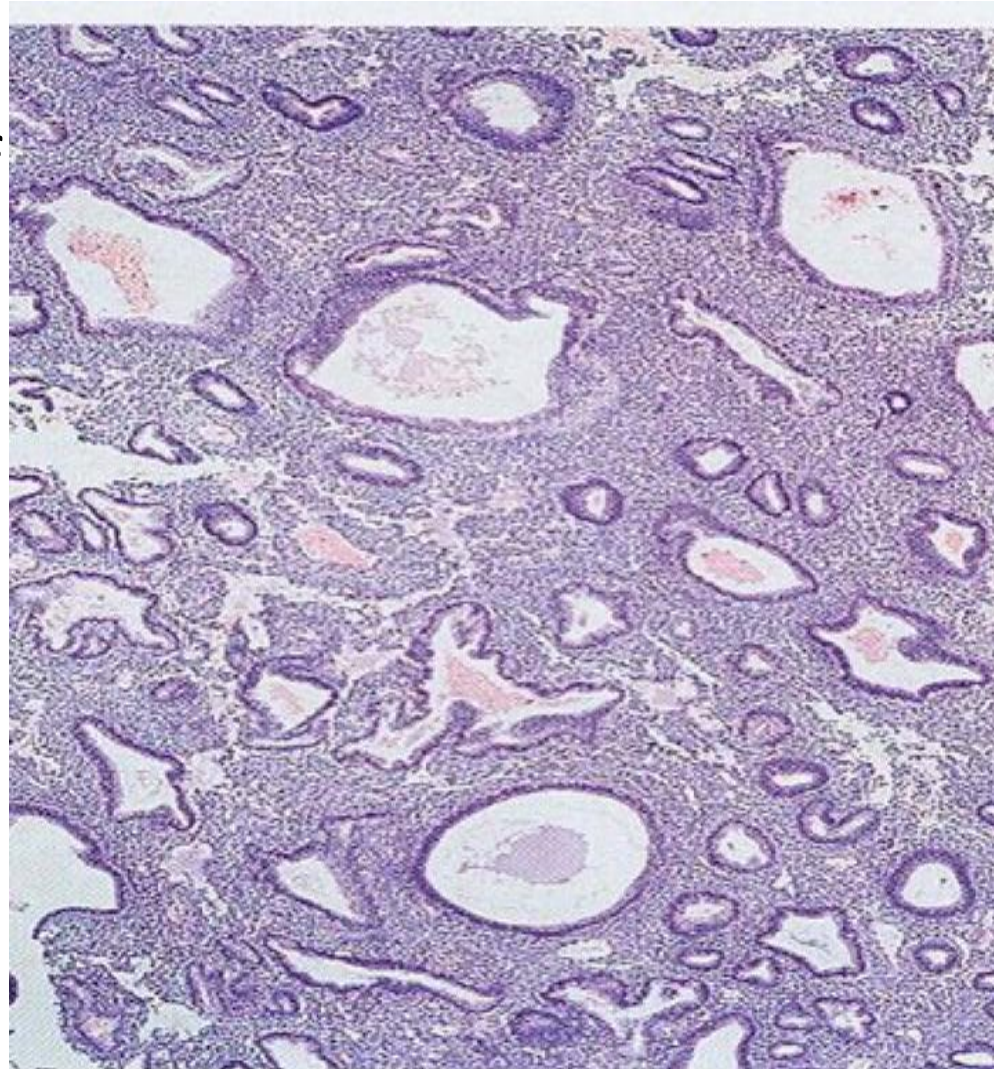
Risk Factors, (estrogen excess)

Estrogen associated risk factor include:

- 1- **Early menarche** or onset of menses(period), **late menopause**, and **nulliparity**(never having given birth).
- 2 - **Diabetes Hypertension Infertility** women tend to be **nulliparous**, often with **anovulatory cycles**.
- 3 - Prolonged **estrogen replacement therapy** without counter balancing progesteron.
- 4 - Estrogen-producing ovarian lesions (**polycystic ovaries**).
- 5 - **Obesity** (because adipose tissue processes steroid precursors into estrogens)

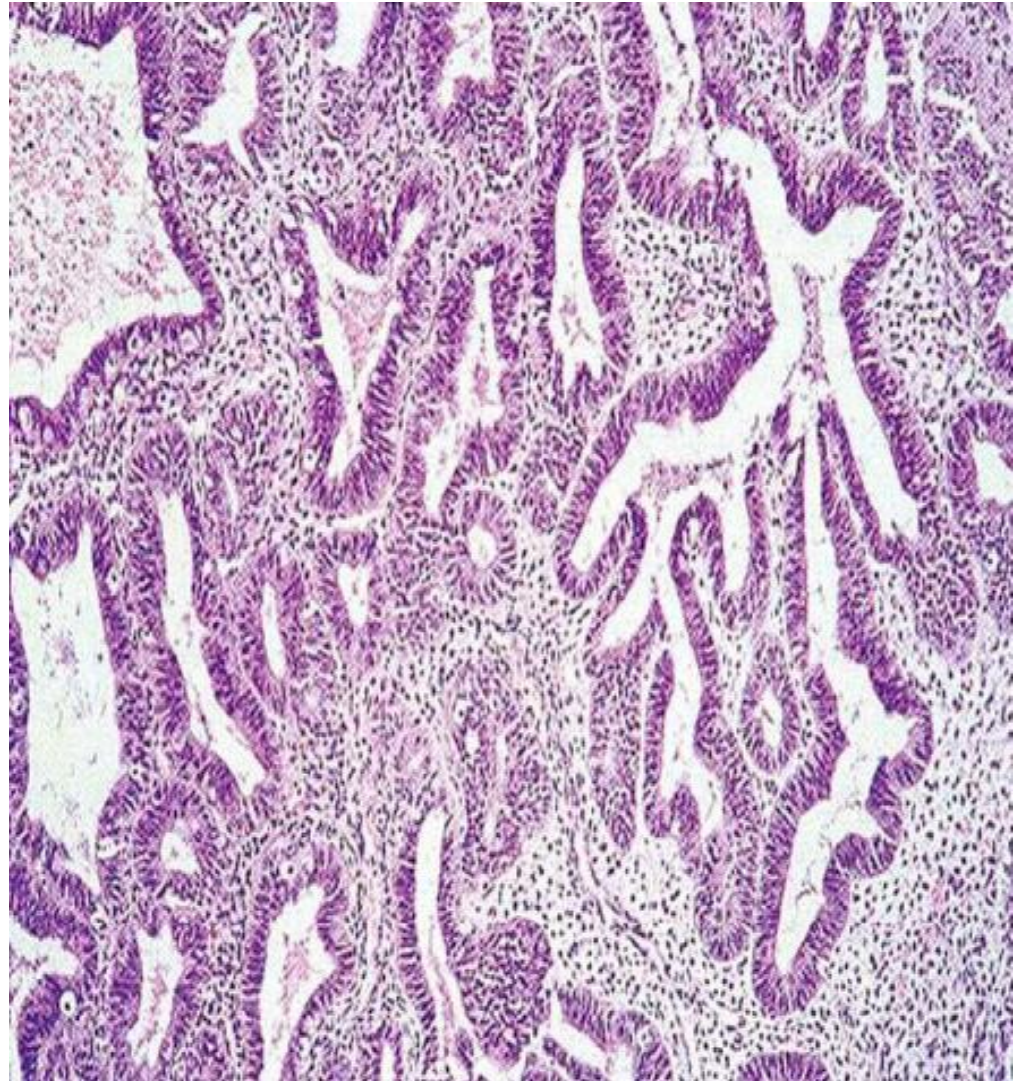
A) Simple hyperplasia

- Crowding of glands **without atypia** some of them are dilated (cystic hyperplasia), **Swiss cheese**.
- Only 1% of cases progress to adenocarcinoma .



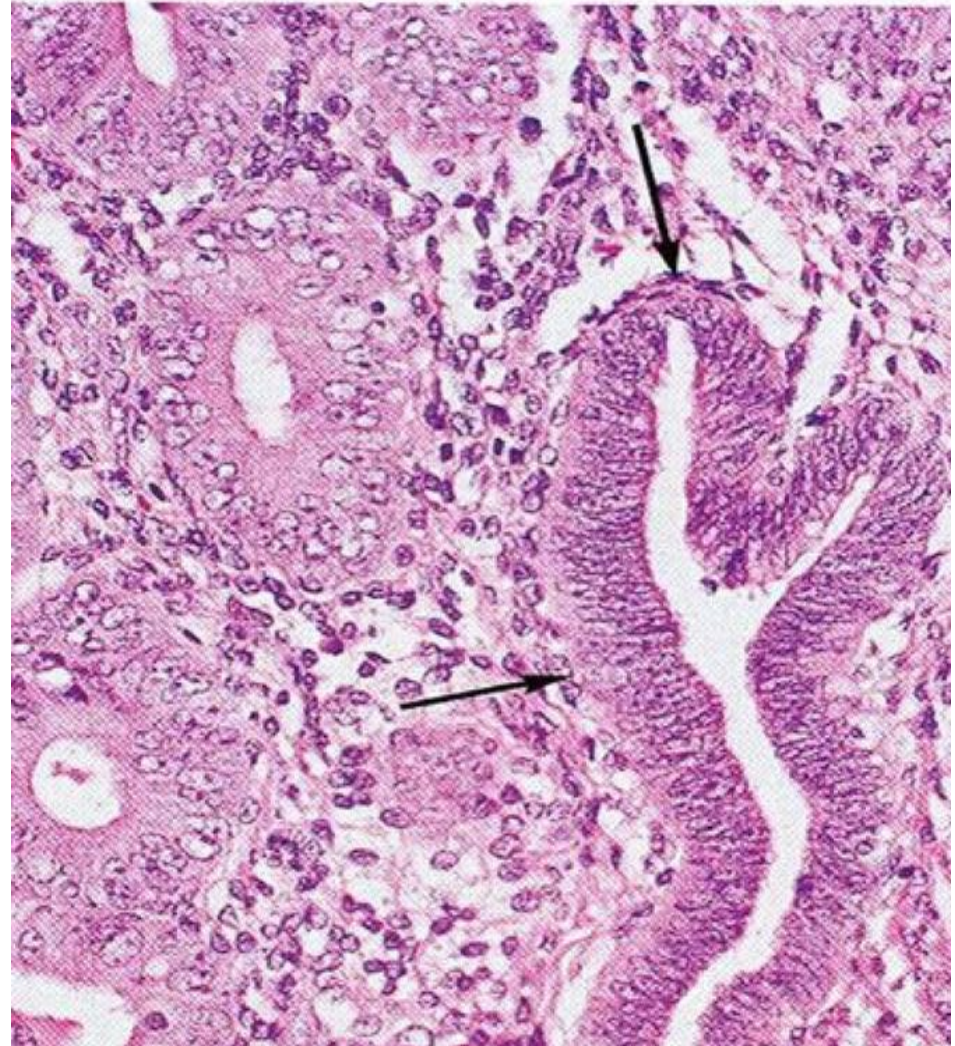
B) Complex hyperplasia

- Crowding of closely packed **branching** glands **without** cellular **atypia**, **Nest like**.
- 3% of cases progress to adenocarcinoma



C) Atypical hyperplasia

- Glandular crowding with atypia (**hyperchromatic nuclei, mitotic figures**).
- Commonly **progresses to adenocarcinoma.**



Endometrial carcinoma

Epidemiology and Pathogenesis:

- The **most frequent** cancer of the female genital tract.
- Common between the ages of **55 and 65 years**
- Two clinical type:
 - 1- In **perimenopausal** women with estrogen excess
(**endometrioid carcinoma**)
 - 2- In **older** women with endometrial atrophy (Less common) but more aggressive (**serous carcinoma**)

Pathogenesis:

1) Endometrioid type:

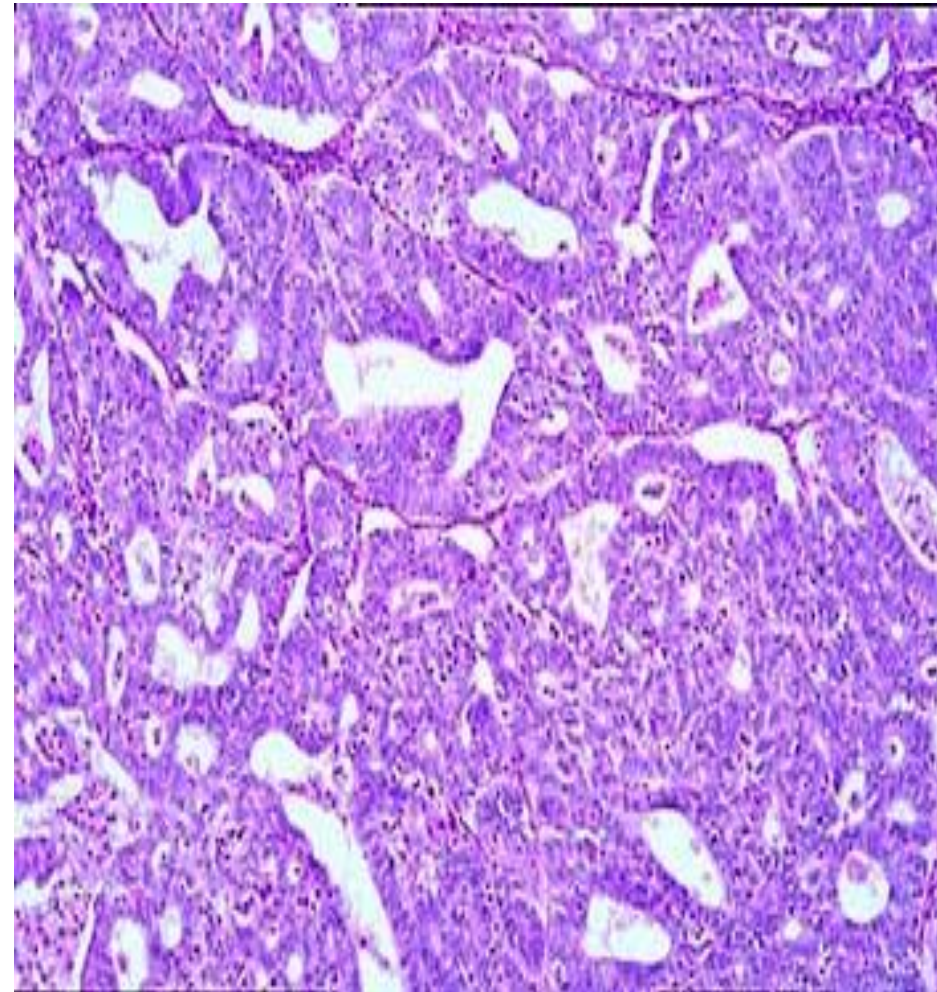
- **Estrogen associated risk factor include:**
- **Endometrial hyperplasia**
- **genetic abnormality:**
mutations in **PTEN**, a tumor suppressor gene

2) Serous type:

- is a distinct type
- It typically arises in a background of **atrophy**
- sometimes arises in **endometrial polyp**
- nearly all cases have mutations in the p53 tumor suppressor gene

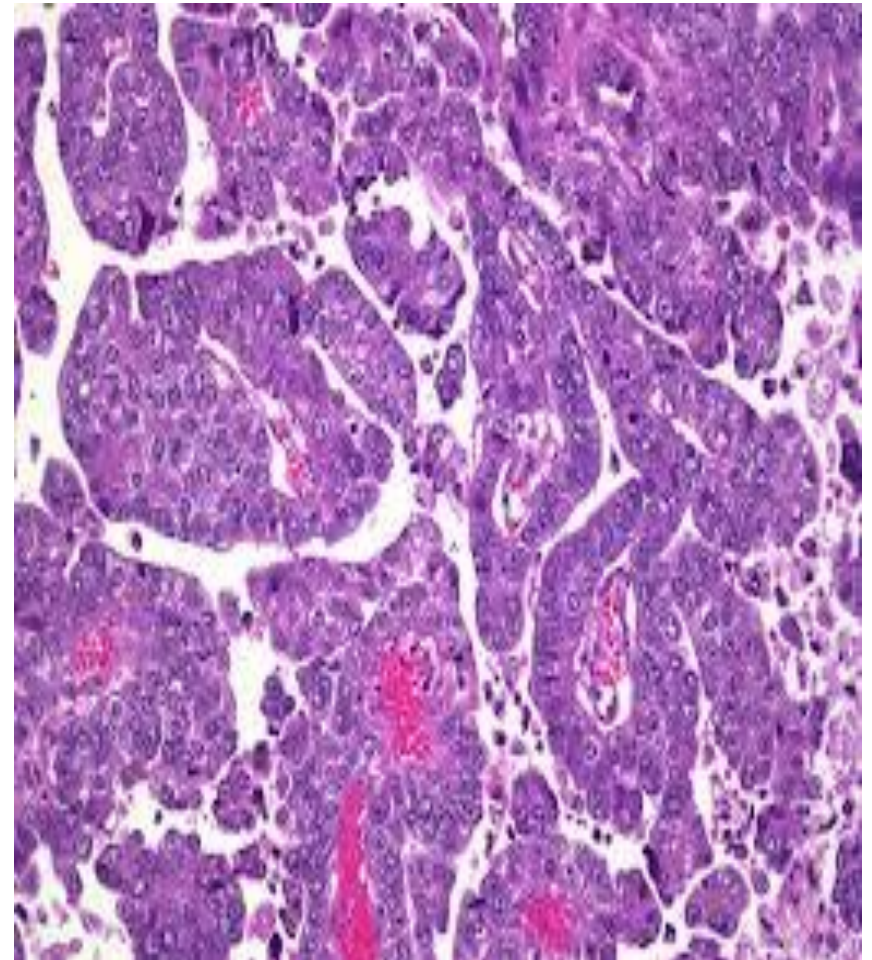
1) Endometrioid type of endometrial carcinoma,

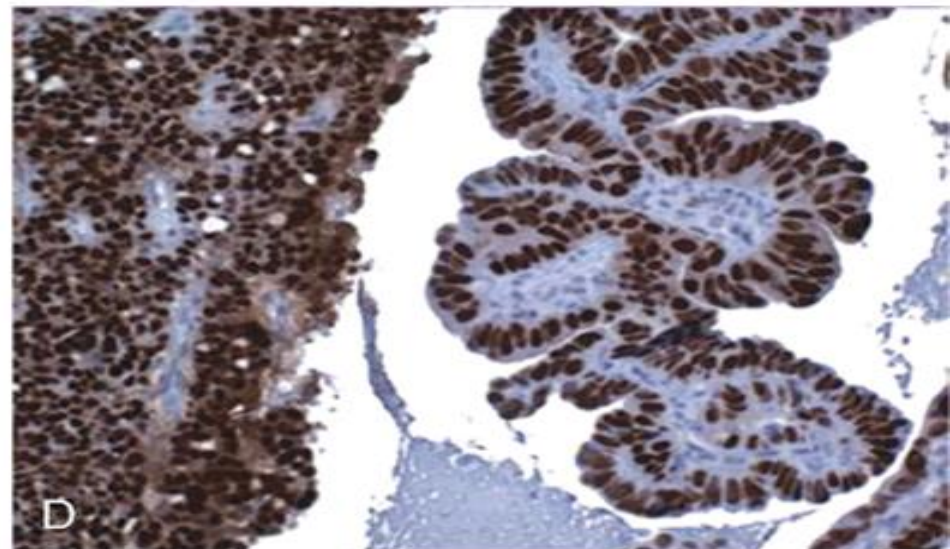
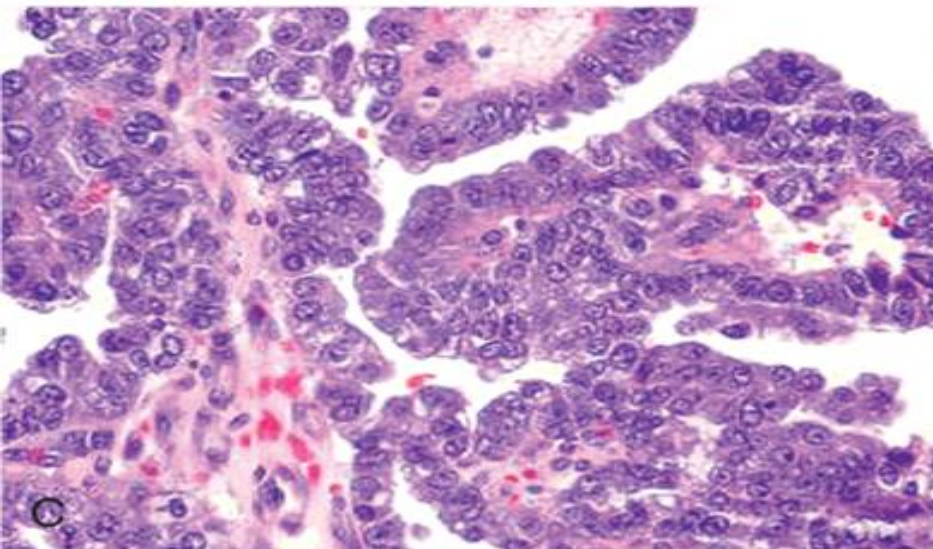
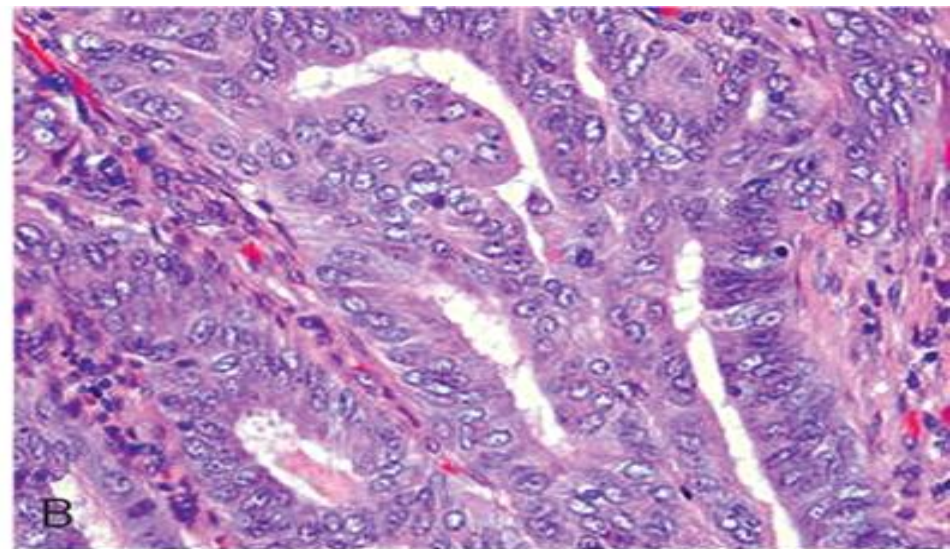
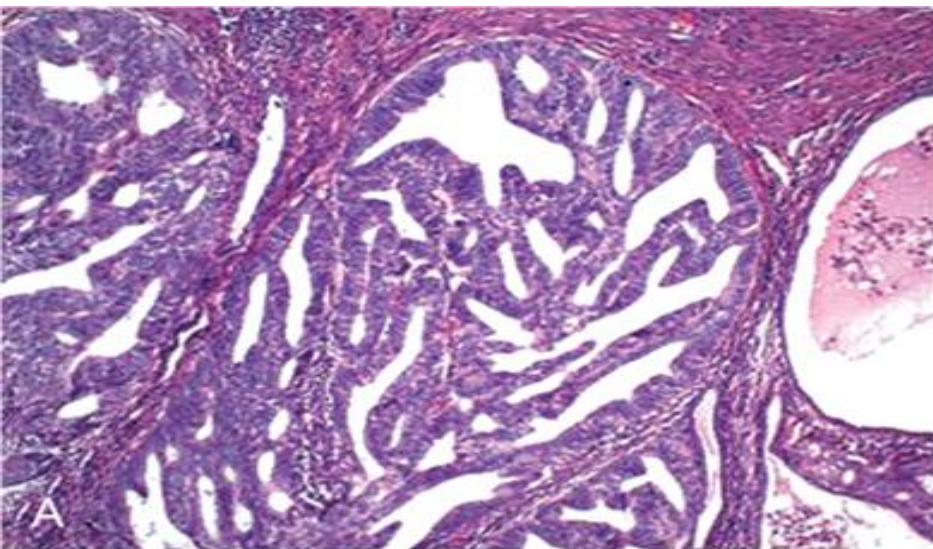
- Closely resemble normal endometrium.
(**Crowded gland with less stroma**).
- **Exophytic or infiltrative**
- Include a range of **histologic types** :
mucinous, tubal (ciliated),
and squamous (occasionally
adenosquamous) differentiation.
- may infiltrate the myometrium and
enter vascular spaces, with metastases
to regional lymph nodes.



2) Serous type of endometrial carcinoma:

- Forms small tufts and **papillae** rather than the glands.
- Has **much greater** cytologic **atypia**.
- They behave as poorly differentiated cancers and are **aggressive**.





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(A, B)Endometrioid carcinoma (C) Serous carcinoma of the endometrium displaying formation of papillae and marked cytologic atypia (D)Immunohistochemical stain for *p53* reveals accumulation of mutant *p53* in serous carcinoma.

Clinical course

- First clinical indication is marked leukorrhea and irregular bleeding .
- With progression, the uterus becomes enlarged and fixed.
- Metastases to cervix, tubes, ovaries, vagina, broad ligament, regional LN, lungs, liver.

Four stages:

stage I: confined to the corpus

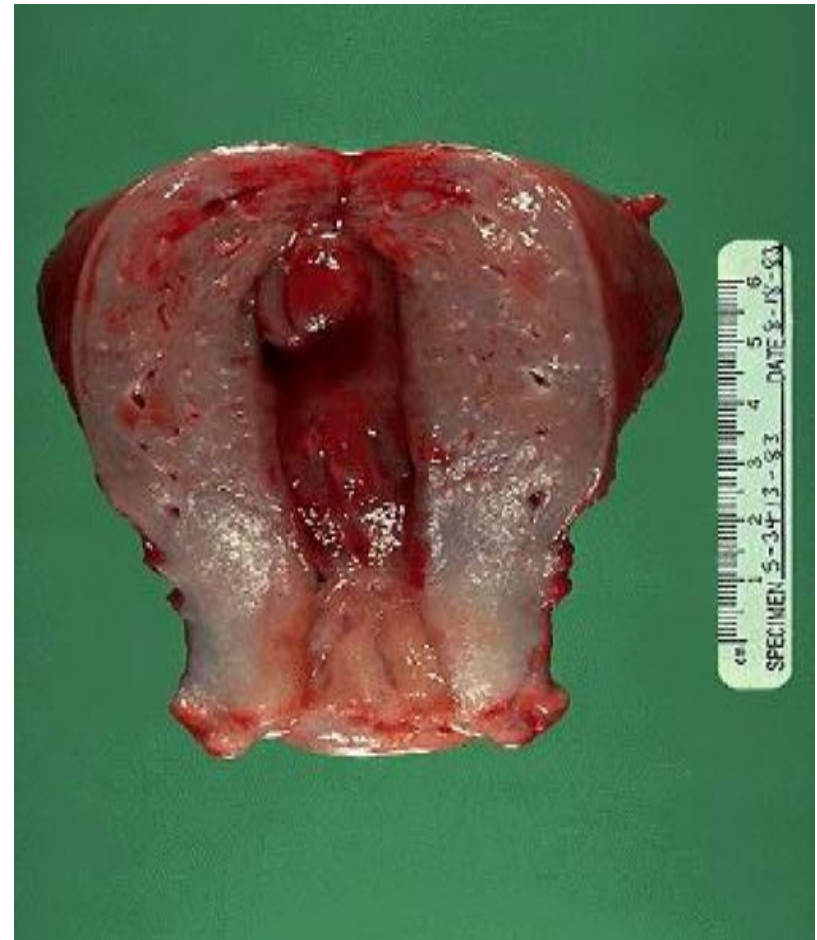
stage II: involvement of the cervix

stage III: beyond the uterus but within the true pelvis

stage IV: distant metastases or involvement of other viscera

Endometrial polyps

- Are focal **benign** overgrowth of endometrium mucosa.
- Most common around the **menopausal** age.
- **Pre-carcinogenic**.
- Most common located on the **fundus**.
- May protrude into vagina and may cause **abnormal bleeding**.
- Endometrial polyp (**fibrous stroma** harboring dilated glands lined by columnar epithelium)



Endometrial polyps; histologic examination

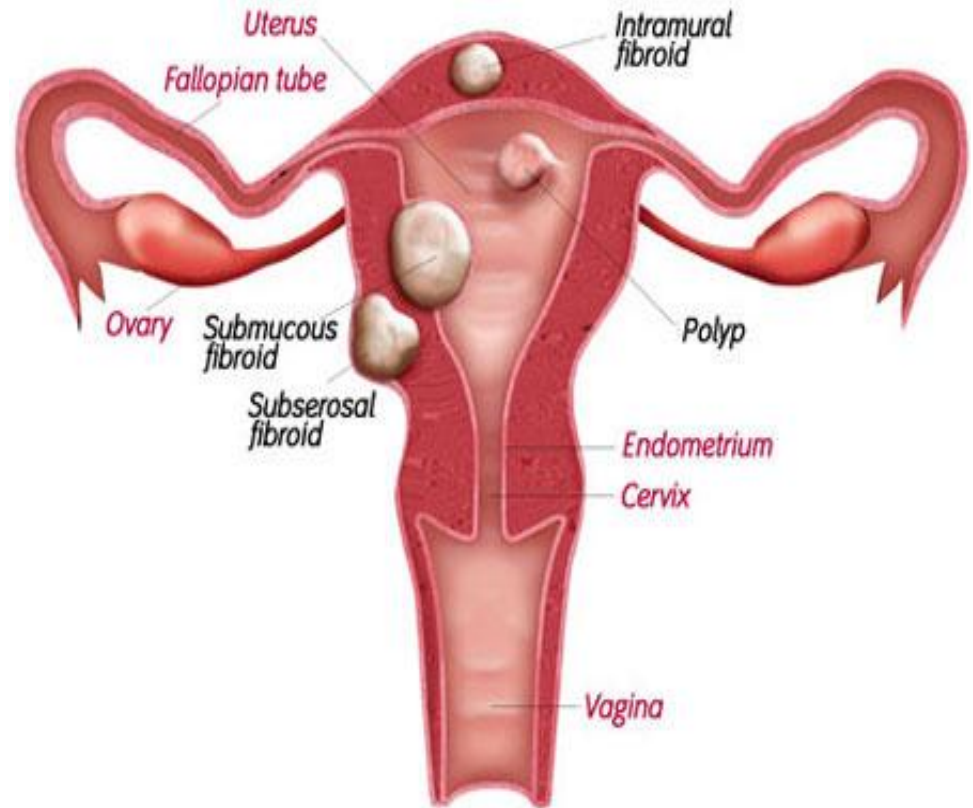
- Composed of endometrium resembling the **basalis** (inactive endometrium), frequently with small muscular arteries. Some glands have a normal endometrial architecture, but more often they are cystically dilated.



Figure 3. Endometrial polyp. Thick walled blood vessels are present within the fibrous core of the polyp. H&Ex50

Leiomyoma (Fibroid)

- The most common **benign** tumor in females of reproductive age.
- arise from the **smooth muscle** cells in the myometrium. May be single or multiple.
- Because of their firmness, however, they often are referred to clinically as **fibroids**.
- Estrogens and possibly oral contraceptives stimulate the growth of leiomyomas; conversely, these tumors **shrink postmenopausally**.



- Some are embedded within the myometrium (**intramural**), lie directly beneath the endometrium (**submucosal**) or directly beneath the serosa (**subserosal**). In the latter location, tumors may spread via blood supply (**parasitic** leiomyomas).

MORPHOLOGY

- **Macroscopic** : Sharply circumscribed, firm gray-white masses with a characteristic whorled cut surface.
- **On histologic examination**, the tumors are characterized by **bundles of smooth muscle cells** mimicking the appearance of normal myometrium. Foci of **fibrosis, calcification, and degenerative** softening may be present.
- Leiomyomas almost **never transform into sarcomas**,



Leiomyosarcomas

- Malignant smooth muscle neoplasia.
- **Not arise from preexisting leiomyomas.**
- in contradistinction to leiomyomas it is **solitary** & usually arise **postmenopausal** women.
- **MORPHOLOGY:**
 - **Macroscopic** : Leiomyosarcomas typically take the form of **soft, hemorrhagic, necrotic masses**.
 - **Histologic appearance** :The diagnostic features of overt leiomyosarcoma include **tumor necrosis, cytologic atypia, and mitotic activity**.
- Recurrence after removal is common with these cancers, and many metastasize, typically to the lungs.

REFERENCE BOOK

- Robbins Basic Pathology : PAGE (691-694)